

Serial Number: Unknown

Filed: Herewith

In the Claims:

Please cancel claims 1-22, without prejudice or disclaimer.

Please add the following new claims:

--23. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of biased randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said biased randomized candidate nucleic acids are biased to minimize stop codons, and wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;
- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
- c) identifying said transdominant bioactive agent.

24. A method for in vitro screening for a transdominant intracellular bioactive agent capable of altering the phenotype of a cell, said method comprising the steps:

- a) introducing a molecular library of biased randomized candidate nucleic acids into a plurality of cells, wherein each of said nucleic acids comprises a different nucleotide sequence, wherein said biased randomized candidate nucleic acids are biased to interact with a class of molecules and wherein said randomized candidate nucleic acids are expressed in said cells to produce a plurality of randomized peptides;
- b) screening said plurality of cells for a cell exhibiting an altered phenotype, wherein said altered phenotype is due to the presence of a transdominant bioactive agent; and
- c) identifying said transdominant bioactive agent.

25. A method according to claim 23 or 24 further comprising the step:

- d) isolating said cell exhibiting an altered phenotype.

26. A method according to claim 25 further comprising the step:

- e) isolating said candidate nucleic acid from said cell.

Serial Number: Unknown

Filed: Herewith

27. A method according to claim 26 further comprising the step:

f) isolating a target molecule using

i) said candidate nucleic acid; or

ii) the expression product of said candidate nucleic acid.

28. A method according to claim 23 wherein said biased randomized candidate nucleic acids comprise codons comprising NNK, wherein N is selected from the group consisting of A, T, C and G, and K is selected from the group consisting of T and G.

29. A method according to claim 24 wherein said biased randomized candidate nucleic acids are biased to interact with a class of molecules selected from the group consisting of SH3 domains, SH2 domains, death domains, enzyme inhibitors, enzyme substrates and protease cleavage sites.

30. A method according to claim 23 or 24 wherein said nucleic acids further comprise a presentation sequence capable of presenting said expression product in a conformationally restricted form.

31. A method according to claim 23 or 24 wherein said introducing is with retroviral vectors.

32. A method according to claim 23 or 24 wherein said cells are mammalian cells.

33. A method according to claim 23 or 24 wherein said library comprises at least 10^4 different nucleic acids.

34. A method according to claim 23 or 24 wherein said library comprises at least 10^5 different nucleic acids.

35. A method according to claim 23 or 24 wherein said library comprises at least 10^6 different nucleic acids.

36. A method according to claim 23 or 24 wherein said library comprises at least 10^7 different nucleic acids.

Serial Number: Unknown

Filed: Herewith

Sub C3
Contd

37. A method according to claim 23 or 24 wherein said library comprises at least 10^8 different nucleic acids.

38. A method according to claim 23 or 24 wherein each of said candidate nucleic acids is linked to nucleic acid encoding at least one fusion partner.

39. A method according to claim 38 wherein said fusion partner is a presentation sequence capable of presenting said expression product in a conformationally restricted form.

40. A method according to claim 38 wherein said fusion partner is a rescue sequence.

41. A method according to claim 38 wherein said fusion partner is a stability sequence.

42. A method according to claim 38 wherein said fusion partner is a dimerization sequence.

43. A method according to claim 38 wherein said fusion partner is a targeting sequence.

44. A method according to claim 43 wherein said targeting sequence is selected from the group consisting of:

- a) a localizing signal sequence capable of constitutively localizing said translation product to a predetermined subcellular locale;
- b) a membrane-anchoring sequence capable of localizing said translation product to a cellular membrane; and
- c) a secretory signal sequence capable of effecting the secretion of said translation product.

45. A method according to claim 44 wherein said targeting sequence is a nuclear localization signal (NLS).

46. A method according to claim 44 wherein said targeting sequence is a myristylation sequence.

Serial Number: Unknown

Filed: Herewith

47. A molecular library of retroviruses comprising at least 10^5 different biased randomized nucleic acids encoding a plurality of biased randomized peptides, wherein said biased randomized candidate nucleic acids are biased to minimize stop codons.

48. A molecular library of retroviruses according to claim 47 comprising at least 10^6 different biased randomized nucleic acids encoding a plurality of biased randomized peptides.

49. A molecular library of retroviruses according to claim 47 comprising at least 10^7 different biased randomized nucleic acids encoding a plurality of biased randomized peptides.

50. A molecular library of retroviruses according to claim 47 comprising at least 10^8 different biased randomized nucleic acids encoding a plurality of biased randomized peptides.

51. A cellular library of mammalian cells containing a molecular library of retroviral constructs, said molecular library comprising at least 10^5 different biased randomized nucleic acids encoding a plurality of biased randomized peptides, wherein said biased randomized candidate nucleic acids are biased to minimize stop codons.

52. A cellular library according to claim 51 wherein said constructs are integrated into the cellular genome.

53. A molecular library of retroviruses according to claim 47, wherein said nucleic acids further encode a fusion partner.

54. A molecular library of retroviruses according to claim 53, wherein said fusion partner comprises a targeting sequence.

55. A molecular library of retroviruses according to claim 53, wherein said fusion partner comprises a rescue sequence.

56. A molecular library of retroviruses according to claim 53, wherein said fusion partner comprises a stability sequence.

Serial Number: Unknown

Filed: Herewith

57. A molecular library of retroviruses according to claim 53, wherein said fusion partner comprises a dimerization sequence.

58. A molecular library of retroviruses according to claim 47, wherein said randomized nucleic acids are biased in their randomization.--